PATENT SPECIFICATION

NO DRAWINGS

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COMPLETE SPECIFICATION

Novel Vitamin Compositions and a process for the manufacture thereof

We, F. HOFFMANN-LA ROCHE & Co., AKTIENGESELLSCHAFT, a Swiss Company of 124—184 Grenzacherstrasse, Basle, Switzerland, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to vitamin compositions and a process for the manufacture thereof. More particularly, the invention is concerned with vitamin compositions containing ascorbic acid and a process for the manufacture thereof. These compositions contain a high level of ascorbic acid and are useful for the production of high potency ascorbic acid tablets.

Tablets which contain ascorbic acid as the active ingredient, as well as processes for producing such tablets, are well known. Ascorbic acid, although crystalline or powdery in nature, cannot be compressed into the tablets without the aid of certain adjuvants and excipients. The quantity of adjuvants and excipients required in any particular instance will vary, depending upon the identity of the materials selected for use. Quite often, however, the adjuvants and excipients will comprise a major portion (for example 50% to 80%) of the weight of the tablets. Such large quantities of excipients and adjuvants are needed to enhance the compressibility characteristics of the granulations and the stability, hardness and disintegration characteristics of the tablets. While the necessity of using large quantities of excipients and adjuvants does not pose a problem which is particularly critical in the case of low potency ascorbic acid tablets, the problem is acute in the case of high potency ascorbic acid tablets. Since large quantities of adjuvants and excipients are required to obtain tablets having completely satisfactory physical characteristics and since high potency tablets require the use of large quantities of ascorbic acid, the tablets must necessarily be rather large. For obvious reasons, the consumer's acceptance of such tablets can be seriously affected.

It has now been found in accordance with the present invention that when a mixture of from 85% to 95% by weight of ascorbic acid of a type hereinafter described and from 5% to 15% of a binder comprising a modified starch, a dextrin, a pregelatinized starch or a mixture thereof (said binder being at least partially soluble in water) is granulated with water, comminuted, dried and subsequently admixed with a tabletting lubricant of the type conventionally used in pharmaceutical tabletting operations, there is obtained a composition capable of being compressed directly into tablets which are relatively small in size and light in weight, which have outstanding physical characteristics and properties and which contain high levels of ascorbic acid.

Accordingly, in one of its embodiments, the invention provides vitamin compositions comprising from 85% to 95% of ascorbic acid of a type hereinafter defined and from 5% to 15% by weight of a binder comprising a modified starch, a dextrin, a pregelatinized starch or a mixture thereof (said binder being at least partially soluble in water).

Ascorbic acid is commercially available in the form of unground crystals or powders. The ascorbic acid which is used in the present invention is in the form of unground crystals 18% to 40% by weight of which are retained on a 200 mesh screen and 60% to 82% by weight of which pass through a 200 mesh screen. Preferably unground crystals 21% by weight of which are retained on a 200 mesh screen and 79% by weight of which pass through a 200 mesh screen are used. The expression "200 mesh screen" denotes a screen having 200 openings per linear inch.

In general, any modified starch, dextrin or pregelatinized starch which is at least partially soluble in water can be employed

in the compositions of this invention. Such materials, which for convenience will be collectively referred to simply as binders, are commercially available from a variety of sources and under various trade names. Thus, for example, there can be used the pregelatinized, modified and stabilized waxy maize starch which is marketed by the National Starch and Chemical Corporation under the trade name "INSTANT CLEARJEL". Furthermore, there can be used the pregelatinized corn starch marketed by the Hubinger Company under the trade name "OK PRE-GEL". Other suitable binders are the pregelatinized food starch (refined from tapioca) marketed under the trade name "INSTANT GEL", the stable modified amylopectin marketed under the trade name "KOSOL", the low viscosity tapioca dextrin marketed under the trade name "CRYSTAL GUM", the dextrinized corn starch marketed under the trade name "PURITY GLAZE" and the cold-water gelling pregelatinized food grade corn starch marketed under the trade designation 78—1215. The foregoing binders are all available commercially from National Starch and Chemical Corporation. The preferred binder is, however, the pregelatinized starch marketed by Corn Products Company under the trade name "AMIJEL".

The compositions comprising the ascorbic acid and the binder are readily manufactured by mixing from 85% to 95% by weight of the ascorbic acid with from 5% to 15% by weight of the binder. In the preferred embodiment of the invention, from 87% to 92% by weight of ascorbic acid are mixed with from 8% to 13% by weight of the binder. The resulting mixture of ascorbic acid and binder can then be granulated in a conventional manner. Water is used as the granulating agent and the quantity employed is variable. Generally, a satisfactory granulation will be obtained using a quantity of water which is equivalent to from 10% to 25% of the weight of the mixture. The granulation is achieved simply by mixing the liquid granulating agent with the mixture of ascorbic acid and binder. The granulation thus obtained can thereafter be passed through a suitable mill or comminuting machine, following which the ground product can be dried at an elevated temperature. After drying, the granulation can be, and preferably is, ground or comminuted once again. Preferably, the granulations which are produced are comprised of particles the sizes of which are distributed approximately as follows: 0.5% are retained on a 16 mesh screen, 17% are retained on a 20 mesh screen, 37% are retained on a 40 mesh screen, 19% are retained on a 60 mesh screen, 9% are retained on a 100 mesh screen and 17.5% pass through a 100 mesh screen. The expressions 16, 20, 40, 60 and 100 mesh screens denote screens having 16, 20, 40, 60 and 100 openings respectively per linear inch.

As mentioned earlier, the compositions described in the preceding paragraphs, after the addition of a tabletting lubricant thereto, are capable of being compressed into high potency ascorbic acid tablets having outstanding physical properties and characteristics and, accordingly, in another of its aspects, the invention provides a composition comprising the aforesaid mixture together with from about 1% to 7% of a tabletting lubricant.

In general, any tabletting lubricant which is conventionally employed in producing pharmaceutical tablets can be used. Thus, for example, the tabletting lubricant can be a stearic acid salt (i.e. a metallic stearate such as magnesium stearate or calcium stearate). Alternatively, a wax-like material (for example, a saturated fatty acid, a mixture containing two or more saturated fatty acids or a hydrogenated glyceride in admixture with a metallic stearate and/or titanium dioxide) can be used. Also suitable for use as the tabletting lubricant is a mixture of 25% by weight of a metallic stearate such as calcium stearate and 75% by weight of corn starch. The preferred tabletting lubricant is a mixture of from 20% to 25% by weight of calcium stearate, from 20% to 25% by weight of silicon dioxide and from 50% to 60% by weight of corn starch. The tabletting lubricant is merely added to, and mixed with, the granulation, following which the mixture can be converted into tablets by conventional methods.

As indicated heretofore, the present invention is based, at least in part, on the use of ascorbic acid in the form of unground crystals having a particular particle size range. The use of powdered ascorbic acid or crystals which are coarser than those defined earlier does not provide a satisfactory product. The invention is noteworthy since it provides compositions which are compressible into tablets using conventional techniques and equipment. The tablets which can be obtained are relatively small in size and light in weight, but at the same time contain a high level of ascorbic acid. For example, in one of the preferred embodiments of the invention, tablets are produced weighing 560 mg to 575 mg and containing 500 mg of ascorbic acid. This is in contrast to conventional 500 mg ascorbic acid tablets which normally weigh from 720 mg to 740 mg. The tablets are of such size that the problem of consumer rejection is, for the most part, obviated. Furthermore, since the tablets contain smaller quantities of inert materials (i.e. excipients and adjuvants) they are far less expensive to produce. Moreover, since tablets produced from the present compositions are lighter in weight and smaller in size than tablets of

comparable potency produced by known methods, smaller and less expensive bottles are required in packaging, storage requirements are minimized and shipping costs are reduced.

The following Examples, in which all parts are parts by weight unless otherwise stated, illustrate the invention:

EXAMPLE 1

200 parts of ascorbic acid and 20 parts of AMIJEL (a pregelatinized corn starch marketed by Corn Products Company) were charged into a stainless steel mixer. The ascorbic acid used was in the form of unground crystals, 29% by weight of which were retained on a 200 mesh screen and 71% by weight of which passed through a 200 mesh screen. The mixture of ascorbic acid and AMIJEL was then granulated using about 25 parts of distilled water. The wet granulation was passed through a Fitzpatrick mill, equipped with a No. 5 screen operating at low speed, with knives forward. The milled granulation was thereafter dried overnight at a temperature of about 40°C. The dry granulation was then passed through a Fitzpatrick mill, equipped with a No. 12 screen operating at medium speed, with knives forward.

The granulation, produced as described in the preceding paragraph, was mixed with a mixture comprising 2 parts of calcium stearate and 6 parts of corn starch. Thereafter, the mixture was compressed into tablets having a weight of 570 mg using a flat-faced, bevelled edged, scored punch.

There were thus obtained tablets each weighing 570 mg and containing 500 mg of ascorbic acid. The tablets had completely acceptable colour, hardness and disintegrating characteristics.

EXAMPLE 2

(a) 500 parts of ascorbic acid in the form of unground crystals 29% by weight of which were retained on a 200 mesh screen and 71% by weight of which passed through a 200 mesh screen were admixed with 25 parts of AMIJEL. This mixture was granulated with distilled water in the manner described in Example 1, following which 5 parts of calcium stearate, 15 parts of corn starch and 5 parts of silicon dioxide were added thereto. The granulation was then compressed, as described in Example 1, into tablets having a weight of 550 mg, each containing 500 mg of ascorbic acid.

The tablets thus obtained were found to possess outstanding colour, hardness and disintegration characteristics.

(b) The procedure described in part (a) of this Example was repeated using 500 parts of the ascorbic acid and 50 parts of AMIJEL. The ascorbic acid used was the same type as was used in part (a) of this example. The granulation was compressed into tablets having a weight of 575 mg, each containing 500 mg of ascorbic acid. The tablets thus obtained were found to have outstanding colour, hardness and disintegration characteristics.

(c) The procedure described in part (a) of this Example was repeated once again using 500 parts of the ascorbic acid and 75 parts of AMIJEL. The ascorbic acid used was of the same type used in part (a). The granulation was compressed into tablets having a weight of 600 mg. The tablets thus obtained each contained 500 mg of ascorbic acid and had outstanding colour, hardness and disintegration characteristics.

EXAMPLE 3

By following the procedure described in Example 2, granulations were prepared using the following named ingredients in the quantities hereinafter indicated:

Gran. No.	Ascorbic Acid (Parts by weight)	Binder (Parts by weight)	Calcium Stearate (Parts by weight)	Silicon Dioxide (Parts by weight)	Corn Starch (Parts by weight)
1	500	25	5	5	15
2	500	50	5	5	15
3	500	75	5	5	15
4	500	25	5	5	15
5	500	50	5	5	15
6	500	75	5	5	15

The ascorbic acid used in each instance was in the form of unground crystals of a particle size such that 29% by weight thereof were retained on a 200 mesh screen and 71% by weight thereof passed through a 200 mesh screen. In the case of Granulation Nos. 1, 2 and 3, the binder employed was the cold-water gelling pregelatinized food grade starch marketed under the designation National Starch 78—1215. In the case of Granulation Nos. 4, 5 and 6, the binder used was the low viscosity tapioca dextrin marketed under the trade name CRYSTAL GUM.

Granulation Nos. 1 and 4 were compressed into tablets weighing 550 mg, Nos. 2 and 5 into tablets weighing 575 mg and Nos. 3 and 6 into tablets weighing 600 mg.

In each instance there were obtained tablets each containing 500 mg of ascorbic acid and having outstanding colour, hardness and disintegrating characteristics.

EXAMPLE 4

Granulations were prepared by the method described in Example 2 using the following ingredients in the quantities hereinafter indicated:

Gran. No.	Ascorbic Acid (Parts by weight)	Binder (Parts by weight)	Calcium Stearate (Parts by weight)	Silicon Dioxide (Parts by weight)	Corn Starch (Parts by weight)
7	500	25	5	5	15
8	500	50	5	5	15
9	500	75	5	5	15
10	500	25	5	5	15
11	500	50	5	5	15
12	500	75	5	5	15

The ascorbic acid used in each instance was in the form of unground crystals 29% by weight of the particles of which were retained on a 200 mesh screen and 71% by weight of the particles of which passed through a 200 mesh screen. In the case of Granulation Nos. 7, 8 and 9, the binder employed was the pregelatinized, modified and stabilized waxy maize starch which is marketed under the trade name INSTANT CLEARJEL. In the case of Granulation Nos. 10, 11 and 12, the binder employed was the pregelatinized food starch refined from tapioca which is marketed under the trade name INSTANT JEL.

Granulation Nos 7 and 10 were compressed into tablets weighing 550 mg, Nos 8 and 11 into tablets weighing 575 mg and Nos 9 and 12 into tablets weighing 600 mg.

In each instance there were obtained tablets having outstanding colour, hardness and disintegration characteristics and each containing 500 mg of ascorbic acid.

EXAMPLE 5

Granulations were prepared by the method described in Example 2 using the following named ingredients in the quantities hereinafter indicated:

Gran. No.	Ascorbic Acid (Parts by weight)	Binder (Parts by weight)	Calcium Stearate (Parts by weight)	Silicon Dioxide (Parts by weight)	Corn Starch (Parts by weight)
13	500	25	5	5	15
14	500	50	5	5	15
15	500	75	5	5	15
16	500	25	5	5	15
17	500	50	5	5	15
18	500	75	5	5	15

The ascorbic acid used in each instance was comprised of unground crystals made up of particles 29% by weight of which were retained on a 200 mesh screen and 71% by weight of which passed through a 200 mesh screen. In the case of Granulation Nos 13, 14 and 15, the binder employed was the stable modified amylopectin which is marketed under the trade name KOSOL. In the case of Granulation Nos. 16, 17 and 18, the binder employed was the pregelatinized starch marketed by A. E. Stanley Manufacturing Company, Decatur, Illinois under the trade name STA—RX 700.

Granulation Nos. 13 and 16 were compressed into tablets weighing 550 mg, Nos. 14 and 17 into tablets weighing 575 mg and Nos. 15 and 19 into tablets weighing 600 mg.

In each instance, there were obtained tablets having outstanding colour, hardness and disintegration characteristics and each containing 500 mg of ascorbic acid.

WHAT WE CLAIM IS:—

1) A vitamin composition comprising from 85% to 95% by weight of ascorbic acid and from 5% to 15% by weight of a binder comprising a modified starch, a dextrin, a pregelatinized starch or a mixture thereof; said ascorbic acid being in the form of unground crystals 18% to 40% by weight of which are retained on a 200 mesh screen and 60% to 82% by weight of which pass through a 200 mesh screen and said binder being at least partially soluble in water.

2) A composition as set forth in claim 1, wherein from 1.0% to 7.0% of a tabletting lubricant is also present.

3) A composition as set forth in claim 2, wherein the tabletting lubricant is a mixture of calcium stearate and corn starch.

4) A composition as set forth in claim 2, wherein the tabletting lubricant is a mixture of from 20% to 25% by weight of calcium stearate, from 20% to 25% by weight of silicon dioxide and from 50% to 60% by weight of corn starch.

5) A composition as set forth in claim 2, claim 3 or claim 4 in the form of compressed tablets.

6) A process for the manufacture of the compositions claimed in any one of the preceding claims, which process comprises intimately mixing from 85% to 95% by weight of ascorbic acid in the form of unground crystals 18% to 40% by weight of which are retained on a 200 mesh screen and 60% to 82% by weight of which pass through a 200 mesh screen with from 5% to 15% by weight of a binder comprising a modified starch, a dextrin, a pregelatinized starch or a mixture thereof (said binder being at least partially soluble in water), granulating the resulting mixture with water, comminuting and drying the resulting granulation, and, if desired, adding a tabletting lubricant and, if further desired, compressing the resulting composition into tablets.

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